REMARKS

Claims 1-16 are pending. Claims 1, 11, 12, 14, 15, and 16 are independent.

Claim Objections

In view of the current amendments to claims 15 and 16, all objections in paragraph 1 on page 2 of the last Office Action are believed to have been overcome.

Summary of the Present Invention

The present invention is an improvement over known methods for particle counting, particularly in counting of a sample of particles having a high density and variability in size. An example prior art approach relied on a variation of the theoretical formula that the counts per second are equal to the inverse of the average period of the particle pulse stream. The known method operates on a principle that wait time contains information about lost counts due to coincidence. For example, based on the known method, if two particles pass through an aperture too close together, the two particles take up to twice as long to go through the aperture. Thus, the known method calculates the average time between particles, or total wait time, of the counted particle stream and sets the corrected count equal to the inverse of the average wait time.

The known method relies on a measured flight time, which is used to calculate the wait time or time the waveform is low. The known method, after mathematical transformation, does not include any term, which represents the time the waveform was high, which is required for a true average period method. A true average period method requires a term which represents the time the waveform is high, and a term that represents the time the waveform was low. Thus, the known method is referred to as a wait time method instead of an average period method.

Applicants in the present invention have found that such previously know method was not effective in handling samples having a wide variety of particle sizes and at high concentrations. The known method is for a sample having a fixed average particle size. If the particle size varies considerably in a sample, the known method based on the calculation of wait time will result in inaccurate counts.

The present invention improves over the known method by providing a method that uses particle size in determining a corrected count. The present invention generates a corrected particle count based on a coincidence correction algorithm that has been enhanced to include an average flight time determined using particle size.

Claim Rejecti n – Claim 15

Claim 15 has been rejected under 35 U.S.C. 102(b) as being anticipated by Farrell et al. (U.S. Patent 4,447,883, hereinafter Farrell). Applicants respectfully traverse this rejection.

Claim 15 has been amended to define true flight-time as being derived based on average channel size. This amendment is based on the description of Figure 1 where it is shown that the average flight time generator 42 has as input the average channel size from the average channel generator 40 (see page 15, second full paragraph). In addition, the invention of claim 15 recites the feature of the invention of basing its particle count determination on three sources of data: raw count of the number of particles, raw wait time between particles, and particle size data.

Farrell, on the other hand, appears to teach a platelet particle count correction method based on average wait time with the additional correction of the Red blood cell count times the average platelet flight time (see equations 1 and 3, columns 3-4). The count correction makes up for errors in detection and counting platelets in the presence of red blood cells in a series of blood samples. Because of their greater size, red blood cells dominate over platelets, resulting in miscounting of platelets. If two particles consisting of a red blood cell and a platelet go through the aperture too close together, then they will take up to twice as long to go through. Thus, the approach in Farrell takes into account the

reduction in the total wait time by increasing the true count. Farrell discloses a formula for determining corrected platelet count that includes a measured platelet mean flight time, Tpm (equation 3). However the platelet mean flight time is multiplied times the red cell count to correct the platelet count from the loss due to red blood cells. Thus, Farrell's formula does not apply to samples with one cell type. Furthermore, Red blood cells and platelets do not typically have significant variation in size. Because each sample in Farrell contains red blood cells and platelets, the approach is for a fixed average particle size; i.e., average particle size is not a factor.

Farrell does mention the case for measurements made for applications wherein dominated particle-dominated particle (i.e., particles of the same type) coincidence errors are significant (i.e., high concentration). For that case, Farrell teaches that the standard coincidence errors correction equation 2 can be used (see column 6, lines 63-68). In other words, Farrell's improved method does not apply to measurements where particles are of the same type at high concentrations; which is a preferred case handled by the present invention.

In particular, the average period method of the present invention preferably handles the case where particles of the same type are of large variation in size and of high concentration. Applicants in the present invention have found that in such case by not taking into account high concentrations and

particle size, if particle size varies considerably in the sample, measured flight time based count would not lead to an accurate particle count. Thus using an approach such as that disclosed in Farrell, the measured platelet flight time used in the formula of Farrell would itself be corrupted by coincidence error.

Therefore, Applicants submit that unlike Farrell, the present claimed invention calculates a true flight time using average channel size. In particular, Applicants submit that Farrell fails to teach or suggest at least, "generating an average channel size from the particle size frequency graph" and "converting the average channel size into a true average flight-time." Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claim Rejection – Claims 1-4, 8-10 and 14

Claims 1-4, 8-10 and 14 have been rejected under 35 USC 103 as being unpatentable over Göhde et al. (U.S. Patent 4,021,117, hereinafter Gohde), in view of Farrell. Applicants respectfully traverse this rejection.

Claims 1 and 14 have been amended to define true average flight time, consistent with the definition provided in the present specification, by including the limitation of, "calculating a true average flight time using said size of each particle." The Office Action admits that Göhde does not disclose a method of processing raw data by using true average flight time and a true

average wait time to obtain a corrected count of particles, and instead relies on Farrell to make up for the deficiency.

Farrell teaches alternative formulas for determining a corrected count for platelets in the presence of red blood cells based on an average wait time method that is modified to include the measured platelet average flight time multiplied by the red cell count. The formulas do not include particle size as a parameter.

Applicants in the present invention have found that by not taking into account particle size, if particle size varies considerably in the sample, flight time based count would not lead to an accurate particle count.

Therefore, Applicants submit that Göhde and Farrell, either alone or in combination, fail to teach or suggest at least, "calculating a true average flight time using said size of each particle." Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claim Rejection – Claims 5-7

Claims 5-7 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Göhde in view of Farrell, and further in view of Carasso et al. (U.S. Patent 6,119,510, hereinafter Carasso).

Claim 5 is directed to the limitation that a sample containing multiple particles of sizes varying by more than 50% is passed through the measuring

chamber, in the context of claim 1's limitation of calculating a true average flight time based on said size of each particle. The Office Action admits that Göhde fails to teach a sample containing multiple particles of sizes varying more than 50%, or wherein particle density variability is greater than 50 fold, and instead relies on Carasso for making up for the deficiency.

Carasso is directed to a method of determining the characteristics of dispersed particles, including determination of particle size distribution for particles ranging in diameter from, for example, about 1 nm to 1000 μm, where particle density can range from 0.1 to 60 volume percent. It makes no reference to particle count correction. Applicants submit that Carrasso does not make up for the deficiency of Göhde and Farrell with respect to claim 1 of failing to teach at least calculating a true average flight time based on said size of each particle. Accordingly, Applicants submit that the rejection fails to establish *prima facie* obviousness for claims 5-7 and respectfully request that the rejection be withdrawn.

Claim Rejection – Claim 11

Claim 11 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Graham et al. (U.S. Patent 6,259,242, hereinafter Graham) in view of Farrell. Applicants respectfully traverse this rejection.

Graham only discloses an apparatus for counting and sizing of particles but does not teach anything specific regarding counting or sizing methods.

The Office Action relies on Graham for disclosing all claimed limitations except for a device for calculating the average flight time of the particles in the sample based on the particle size signal and the particle number signal; or a correcting unit for correcting an apparent particle count to an adjusted particle count by adding a true average flight time to a true average wait time to obtain a corrected count of particles. Instead, the Office Action relies on Farrell for making up for the deficiency.

Farrell's formula appears to take into account a measured flight time Tpm, but does not include a parameter for particle size. In particular, Applicants submit that Farrell does not disclose a "particle size signal." Thus, Applicants submit that Fearrell does not teach or suggest at least calculating an average flight time of particles based on the particle size signal and particle number signal. Therefore Graham and Farrell, either alone or in combination, fail to teach at least, "a device for calculating an average flight time of said particles in said sample based on said particle size signal and said particle number signal." Accordingly, Applicants submit that the rejection fails to establish *prima facie* obviousness for claim 11 and respectfully request that the rejection be withdrawn.

Claim Rejection – Claims 12 and 13

Claims 12 and 13 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Gear (U.S. Patent 4,090,129) in view of Jones, Jr. (U.S. Patent 5,452,237). Applicants respectfully traverse this rejection.

The Office Action relies on Gear for disclosing the claimed invention except for the program for processing raw data from the detector, the program having the capability to add true average flight time to average wait time to give a true average period value. Instead the Office Action relies on Jones, Jr. for making up for the deficiency.

Gear discloses an apparatus used for determining platelet aggregation and does not teach particle sizing or counting methods.

Jones, Jr. discloses a method for improving the accuracy of red blood cell MCV or mean cell volume measurements. This is the average size of red blood cells. The MCV is derived from a particle size frequency graph or histogram. As the red cell concentration increases the MCV also falsely increases due to particle coincidence. This method improves the red blood cell size histogram by coincidence correcting each channel. This method deals with improving particle size determination and does not apply to particle counting.

Jones, Jr. discloses an improved method for correcting for coincidence

errors, where the measured particle distribution is of a particle population having various particle sizes (section, "Field of the Invention"). Jones, Jr. teaches a multi channel particle counter and correction by at least a first correction factor and a second correction factor (section, "Summary of the Invention"). A channel counter 22 determines for each of the quantization channels the number of particles registered in each channel (column 3, lines 6-9). An over_count is defined as, for example with respect to a particle size 7, the coincidence of a size 6 particle with a size 1 particle, the coincidence of a size 5 particle with a size 2 particle, etc. In the multi-channel particle size counting system, over_count is corrected by reducing the measured probability for the count for that particular channel, by the probability of the over_count (column 4, lines 52-57). An undercount would occur in the case where the particle of a particular size inconsistent with the proper channel is not counted in its proper channel (column 4, lines 58-62). The actual count of a channel is approximated by taking into account the probability of over_count and the probability of undercount for that channel (column 5, lines 5-19). In particular, both correction factors are added to, or subtracted from the measured average wait time (termed dead time; see column 3, lines 45-65, especially expression (2); column 5, lines 27-43).

Unlike the method in Jones, Jr., the present claimed invention calculates

a true average flight time using the size of particles. Also, unlike the method in Jones, Jr., the present claimed invention adds true average flight time to average wait time to give a true average period value. Thus, Applicants submit that Gear and Jones, Jr., alone or in combination, fail to teach at least the claimed "program adding true average flight time to average wait time to give true average period value" in the context of a true average flight time calculated using the size of the particles. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claim Rejection – Claim 16

Claim 16 has been rejected under 35 U.S.C. 103(a) as being unpatentable over Farrell in view of Berg et al. (U.S. Patent 5,247,461, hereinafter Berg). Applicants respectfully traverse this rejection.

The Office Action relies on Farrell for teaching the claimed invention, except for the claimed coincidence-corrected count generator, and instead relies on Berg for making up for the deficiency.

Specifically, the Office Action alleges that Farrell teaches an average period count generator, i.e., equation 3 for calculation of a corrected platelet count P. Further, the Office Action alleges that Berg teaches a coincidence-corrected count generator, i.e., unit 28 which applies coincidence corrections to a data

array of partial results for each of the channels and produces an array of corrected particle size distribution of the sample.

Berg teaches a method to improve the particle size frequency distribution graph or size histogram. Berg only teaches correcting the counts in the channels of the particle size histogram. Berg does not address coincidence correction of the total particle cell count.

Berg's coincidence corrections include an amount by which the number of particles sensed for each particle size classification must be increased or decreased to account for coincidence of exactly two particles within the sensing zone, and to account for the presence of three particles at one time (column 10, lines 59-67).

Because P is a corrected platelet count, applying the teachings of Berg effectively implies applying Berg's coincidence corrections to Fearrell's corrected platelet count to arrive at a true count of the number of platelets. The Office Action alleges that such a combination would increase the efficiency of the measurement procedure. Applicants disagree.

Applicants submit that one of ordinary skill in the art would not have been motivated to combine the teachings of Berg and Fearrell, at least because Fearrell's corrected platelet count has already been accurately corrected for coincidence errors (Ferrell at column 4, lines 1-6). Furthermore, Applicants

submit that at most, Berg teaches an alternative approach to correcting for coincidence errors to that in Ferrell. Thus, Applicants submit that Ferrell and Berg, either alone or in combination, fail to teach at least the claimed coincidence-corrected count generator. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Summary

In summary, it is respectfully submitted that all grounds of rejection have been overcome by argument or amendment and that the Examiner would be justified in passing the case to issue. Such action is earnestly solicited.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit

Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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